REMARKS

Applicants respectfully request entry of the foregoing amendments and reconsideration of the subject matter identified in caption, as amended, pursuant to and consistent with 37 C.F.R. §1.112, and in light of the remarks which follow.

Claims 1 and 3-16 are pending in the application. Applicants hereby amend the claims to address certain ambiguities associated with transitional phrases as identified by the Examiner, and to follow the style and format conventions of U.S. practice.

Claims 1 and 7 are hereby cancelled, and claim 2 has been previously canceled. The substance of claim 1 has been rewritten and is hereby introduced as claim 17. The claim is rewritten to enhance clarity, to eliminate potential ambiguities associated with transitional phrases, and to eliminate artifacts from translation of the original claims from French. The amendments are not necessary to distinguish over the cited art, but merely to more clearly point out and distinctly claim what Applicants' regard as their invention.

Applicants also add new claim 18, which recites the tablet of claim 17, but with the addition of a coating on the exterior of the tablet (not the neutral microgranules). Coatings are those that can modify appearance, or the transmission of gas (O_2), moisture or light, or a gastroresistant coating to modify the release of the active principle. Support for such coatings is found at page 13, line 35 to page 14, line 4.

Applicants submit that the amended and added claims add no new matter and overcome the rejection based upon 35 USC § 112, second paragraph.

Prior Art Rejections:

The Makino reference purportedly teaches spherical granules having a core coated with a powder containing a drug and HPC. The granules reportedly have excellent hardness and disintegration properties, i.e., mechanically robust and resistant to breaking or scraping in a CF granulator ("centrifugal-Fluiding granulator"). Col. 1, lines 44-54.

The spherical granules have a core, such as Nonpareil, and a coating layer. The coating layer is applied to the core by spraying a powder containing a drug and L-HPC with an aqueous binder onto said core. Col. 1, lines 55-63.

The spherical granules may be further coated with a sustained-release coating, a gastric coating, an enteric coating, or taste-masking coating. Col. 4, lines 15-19 and lines 30-34.

Makino, however, is directed to the preparation of granules for use as they are or in capsules. Col. 1, lines 8-14. Makino does not teach that the spherical granules are directly compressible, nor that they are suitable for being compressed into tablets. The Official Action expressly acknowledges that Makino does not teach a tablet formulation. Indeed, Makino distinguishes the use of granules in capsules from tablet compositions. Col. 1, lines 15-18. Thus, one skilled in the art would understand that Makino is limited to the preparation of spherical granules for use on their own or in capsules, but not in tablets.

Koyama does not provide the missing teaching, motivation or suggestion to modify Makino in such a way that one would have arrived at the claimed invention. Indeed, Koyama teaches that in order to compound a formulation suitable for tableting, one must add a very substantial quantity of additional ingredients.

In view of Makino's express distinction between capsules and tablets, one skilled in the art would not have been motivated to compound the formulation of Makino into a tablet. Moreover, there would have been no motivation or suggestion to combine Makino's formulations with the compositions of Koyama to produce a tablet. And, even if one were so motivated, there is nothing in either of the references to suggest that the resultant product would be that as now claimed by Applicants. Indeed, as discussed below, Koyama teaches that the use of its granules in any composition suitable for tableting would require very substantial additional excipients that far exceed the allowable limitations for such excipients in the present claims.

The Koyama reference purportedly teaches the fabrication of granules containing an active principle using a centrifugal fluidized-bed coating granulator ("CF granulator"). CF granulators are acknowledged as presenting challenges in that they damage the spherical granules. Page 2, lines 28-36.

Koyama reports that spraying seed granules with a dispersion of low-substituted hydroxypropylcellulose (L-HPC) can produce spherical granules having enhanced granule strength and improved disintegrating property. Page 2, lines 37-46.

Koyama reports the preparation of granules having a neutral core, onto which is sprayed a solution containing L-HPC, an active principle and other excipients (see examples 3 or 4). The granules may be covered with an enteric coating (see examples 1, 2 or 5).

Koyama does suggest that the granules can be mixed with other components to produce a formulation suitable for compression into tablets. Page 4, lines 5-6.

However, the only example (Example 2) disclosing the preparation of a tablet requires substantial additional ingredients, and is quite distinct from the tablets and compositions disclosed and claimed here.

In Koyama's Example 2, the tablets are formed by compression of a mixture comprising:

- 420 g of enteric-coated granules of Serrapeptase sprayed onto neutral cores,
- 270 g of aluminum hydroxide sodium hydrogeno-carbonate coprecipitate,
- 580 g of crystalline cellulose,
- 150 g of magnesium stearate, and
- 1440 g of granules for tablet compression (prepared by granulating a mixture of various ingredients, but not spraying a coating onto neutral cores).

The "granules for tablet compression" are fabricated according to a method described at p. 5, lines 46-56. The granules comprise substantial additional ingredients including excipients already found in substantial quantities above such as crystalline cellulose.

Koyama does not teach compression of the granules claimed here with less than 1% by weight of compression excipients. Koyama's Example 2 includes in particular "granules for tablet compression", which represent around 50% of the tablet weight and crystalline cellulose (a diluent), which represents around 20% of the tablet weight.

Koyama does not teach the preparation of tablets from granules consisting essentially of neutral microgranules of sucrose and starch which are coated only with an active agent and optional binder, and less than 1% of optional compression excipient. Applicants have now recited that the tablet, per se, consists essentially of only those ingredients.

There is no suggestion in Koyama that in the absence of the various and substantial compression excipients, those formulations can be successfully compressed into tablets; nor is there any suggestion in either of the cited references that the formulations of Makino can be successfully compressed into a tablet. Indeed, Koyama teaches away from such a combination by showing that various and substantial additional ingredients are required to make the disclosed formulations compressible into tablets. Thus, applicants' amended claims would not have been obvious over Makino in combination with Koyama.

In view of the foregoing amendments and remarks, applicants respectfully request reconsideration and withdrawal of all outstanding rejections. Applicants submit that the claims are now in condition for allowance, and respectfully request formal notification to that effect. If, however, the Examiner perceives any impediments to such a notice of allowability, whether substantive or formal, the Examiner is encouraged to call Applicants' attorney at the number provided below. Such informal communication will expedite examination and disposition of this case.

Respectfully submitted,

BUCHANAN INGERSOLL & ROONEY PC

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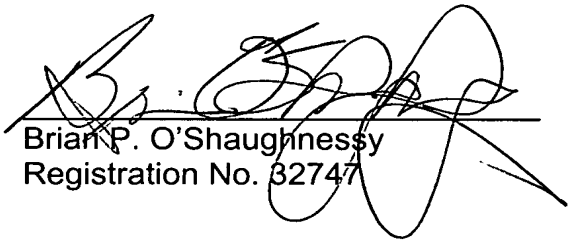
By: 

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